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Definitions and forms of primary, genetic HCM

Hypertrophic cardiomyopathy (HCM) is a clinical heterogeneous cardiac disease that is in most cases inherited as an autosomal dominant trait. According to the classification of the American Heart Association (AHA), HCM is a primary genetic heart disease. HCM is morphologically characterized and defined as a hypertrophied, non-dilated left ventricle (LV) without any underlying systemic or cardiac disease that could cause LV hypertrophy (LVH), like systemic hypertension or (sub-)aortic stenosis. HCM is usually a progressive disease that finally leads to congestive heart failure (CHF) or sudden death, however, the degree of hypertrophy and the velocity of the progression is highly variable with some affected individuals dying very young, and others remaining in a compensated state until old age. Diagnosis is usually based upon two-dimensional (2D) echocardiography.
In humans and cats the echocardiographic picture is very heterogeneous concerning the severity of LVH and myocardial hyperechogenicity as well as the localisation of LVH. The hypertrophy may be symmetrical (global) and assymetrical (regional). The symmetric form affects the LV homogenously, whereas the asymmetric form involves selectively only the papillary muscles, the LV posterior wall, the interventricular septum (IVS) as a whole or only focally just below the aortic valve. Systolic anterior motion of the mitral valve (SAM) is common in HCM, and for this dynamic subaortic stenosis the term hypertrophic obstructive cardiomyopathy (HOCM) was created. Secondary obstruction of the LV outflow tract (LVOT) may worsen LV hypertrophy through additional pressure overload.

HCM → SAM; SAM = HCM ?

The development of SAM has commonly been attributed to LVH, narrowing of the LVOT and drag forces acting on the anterior mitral valve leaflet, i.e. SAM has been considered a complication or consequence of HCM. However, in some cats with SAM it has been observed that both SAM and LVH disappeared under treatment with betablockers. Furthermore SAM may be observed in very young or quite old cats without any LVH, when echocardiography is performed to detect the source of a (new) murmur. These observations imply that SAM may be a primary problem that may cause secondary LV hypertrophy. A similar albeit rare phenomenon has been described in dogs by D'Agnolo and others. The question arises concerning the development and the classification of this entity; experimentally, SAM can be produced by displacement of the anterior papillary muscle. Possibly, the cause of "primary

SAM" is different in young, and in older cats. In young cats a congenital abnormality of the anterior papillary muscle resulting in an abnormal attachment of the chordae tendineae and mitral valve may be the cause; this entity probably should be classified as mitral valve dysplasia. In older cats with a new heart murmur and "primary SAM", myocardial and especially papillary muscle remodeling secondary to inflammatory, toxic, or ischemic insults may responsible. These entities should rather be classified as secondary cardiomyopathies.

Myokarditis versus HCM

Myocarditis is known to cause abnormal myocardial function and cardiac dilation in humans for many years. Many cases of dilated cardiomyopathy (DCM) are actually caused by myocarditis. In humans, myocarditis is therefore classified as primary mixed cardiomyopathy. Myocarditis in cats is also well recognized. Interestingly, in affected cats echocardiography usually often does not show DCM but LVH. In a recent pathological study, cats with cardiomyopathy were examined by histology and by PCR. 55 % of the cats with HCM showed signs of active myocarditis on histology, and parvovirus was found in some. The authors have examined several cats that had developed pulmonary oedema associated with anaesthesia or surgery, and that on echocardiography had shown LVH and left atrial dilation typical of HCM. Supportive therapy including diuretics and oxygen led to resolution of the congestion and clinical normalisation. Repeated echocardiography showed a successive regression of LVH and LA dilation. This presentation and disease course argue against primary HCM, but rather for a reversible damage like infectious or toxic myocarditis.

Steroid-induced **„HCM“**

A similar picture as in the suspected myocarditis cases with acute congestive heart failure has been reported in cats after the application of steroids. Such cats, initially diagnosed with HCM due to LV hypertrophy and LA dilation did not only recover clinically from congestive heart failure but did also normalize echocardiographically. Nevertheless, attempts to elicit this form of cardiomyopathy experimentally were unsuccessful. The question arises, if a genetic predisposition is required to react in this fashion to steroids, or alternatively if affected cats in fact had myocarditis associated with glucocorticoid application.

Hyperthyroidism-induced cardiomyopathy

Thyroid hormones have important metabolic and cardiovascular effects. Hyperthyroidism causes an increased metabolic rate which demands an increased cardiac output. In the periphery thyroid hormones cause a decreased vascular resistance. In the myocardium, thyroid hormones induce multiple genes causing LV hypertrophy. Echocardiographically, these

pathophysiological changes are expected to be reflected by LV volume overload, respectively eccentric LVH. However, concentric hypertrophy secondary to hyperthyroidism has been reported as well

Myocardial hypertrophy caused by infiltrations

Infiltrative myocardial diseases like amyloidosis have not been reported in veterinary medicine. Rarely, diffuse neoplastic infiltrations are found in malignant lymphoma that on echocardiography look similar to LVH, respectively HCM.

HCM as cause of systemic hypertension (?)

Occasionally, HCM has been reported as differential diagnosis for systemic hypertension. However, as blood pressure is a function of cardiac output and peripheral resistance, there is no rational explanation for such a relationship. LVH with or without CHF associated with truly elevated blood pressure has to be considered consequence and not cause of the hypertension. Likewise, if LVH is found echocardiographically and HCM suspected, systemic hypertension should be ruled out before HCM is diagnosed.

Pseudohypertrophy

Like with any hollow organ in the body, the wall thickness of the heart physiologically changes as a function of its filling, e.g. the wall is thinner in diastole and thicker in systole. Similarly, with (iatrogenic) hypervolemia there will be an increase in ventricular and atrial size and decrease in wall thickness, with dehydration cardiac size will decrease and wall thickness will increase.

When HCM looks like DCM - the "burn out" cardiomyopathy

In some case of feline (and human) HCM a regression of the LV hypertrophy can be seen during disease progression. The myocardial wall gets thinner, the LV volume becomes overloaded and progressive systolic dysfunction develops. It may be difficult to differentiate this echocardiographic picture from DCM, unless the patient has been examined and diagnosed at previous examinations with HCM. This presentation is considered end stage HCM and is called "burn out" cardiomyopathy.

Synopsis

Based on the above explanations, the following aspects should be considered when echocardiographically LVH is found, and before HCM is diagnosed:

- Is the LVH only a pseudohypertrophy secondary to hypovolemia?

- Is a fixed or dynamic (sub-) aortic stenosis present?
- Is systemic hypertension present?
- Did the cat receive steroids, is there a history of recent anaesthesia, or is systemic, potentially bacterial, disease present?
- Does the cat have hyperthyroidism?

If any of these questions is answered with "yes", treatment should be started according to the underlying disease. If on follow-up examinations echocardiographic changes are reversible, the cat does not have primary HCM.

To summarize, several myocardial diseases can look like HCM on echocardiography. Only clinical and echocardiographic follow-up examinations allow the differentiation between primary HCM and secondary left ventricular wall thickening. Various diseases looking like HCM but which are curable should be considered and treated accordingly, before a cat with congestive heart failure is diagnosed with HCM, a genetic, progressive, non-curable, and ultimately fatal heart disease.

References

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